

## 1. Go Fish



To an aspiring animal owner, Petco presents an embarrassment of riches. Here, in the basement of a New York City store—where the air carries the sharp tang of hay and the dull musk of rodent dander—is a squeaking, squealing, almost endless menagerie of potential pets. There are the spindly-legged lizards scuttling across their sand-filled tanks; the preening cockatiels, a spray of golden feathers atop their heads; and, of course, the cages of pink-nosed white mice training for a wheel-running marathon. There are chinchillas and canaries, dwarf hamsters, tree frogs, bearded dragons, red-footed tortoises, red-bellied parrots, and African fat-tailed geckoes.

But one of these animals is not like the others. The discerning pet owner in search of something new and different merely has to head to the aquatic display and keep walking past the speckled koi and fantail bettas, the crowds of goldfish and minnows. And there they are, cruising around a small tank hidden beneath the stairs: inch-long candy-colored fish in shades of cherry, lime, and tangerine. Technically, they are zebrafish (*Danio rerio*), which are native

to South Asian lakes and rivers and usually covered with black and white stripes. But these swimmers are adulterated with a smidgen of something extra. The Starfire Red fish contain a dash of DNA from the sea anemone; the Electric Green, Sunburst Orange, Cosmic Blue, and Galactic Purple strains all have a nip of sea coral. These borrowed genes turn the zebrafish fluorescent, so under black or blue lights they glow. These are GloFish, America's first genetically engineered pets.

Though we've meddled with many species through selective breeding, these fish mark the beginning of a new era, one in which we have the power to directly manipulate the biological codes of our animal friends. Our new molecular techniques change the game. They allow us to modify species quickly, rather than over the course of generations; doctor a single gene instead of worrying about the whole animal; and create beings that would never exist in nature, mixing and matching DNA from multiple species into one great living mash-up. We have long desired creature companions tailored to our *exact* specifications. Science is finally making that precision possible.

Though our ancestors knew enough about heredity to breed better working animals, our ability to tinker with genes directly is relatively new. After all, it wasn't until 1944 that scientists identified DNA as the molecule of biological inheritance, and 1953 that Watson and Crick deduced DNA's double helical structure. Further experiments through the '50s and '60s revealed how genes work inside a cell. For all its seeming mystery, DNA has a straightforward job: It tells the body to make proteins. A strand of DNA is composed of individual units called nucleotides, strung together like pearls on a necklace. There are four distinct types of nucleotides, each containing a different chemical base. Technically, the bases are called adenine, thymine,

guanine, and cytosine, but they usually go by their initials: A, T, C, and G. What we call a "gene" is merely a long sequence of these A's, T's, C's, and G's. The order in which these letters appear tells the body which proteins to make—and where and when to make them. Change some of the letters and you can alter protein manufacturing and the ultimate characteristics of an organism.

Once we cracked the genetic code, it wasn't long before we figured out how to manipulate it. In the 1970s, scientists set out to determine whether it was possible to transfer genes from one species into another. They isolated small stretches of DNA from *Staphylococcus*—the bacteria that cause staph infections—and the African clawed frog. Then they inserted these bits of biological code into *E. coli*. The staph and frog genes were fully functional in their new cellular homes, making *E. coli* the world's first genetically engineered organism. Mice were up next, and in the early 1980s, two labs reported that they'd created rodents carrying genes from viruses and rabbits. Animals such as these mice, which contain a foreign piece of DNA in their genomes, are known as transgenic, and the added genetic sequence is called a transgene.

Encouraged and inspired by these successes, scientists started moving DNA all around the animal kingdom, swapping genes among all sorts of swimming, slithering, and scurrying creatures. Researchers embarking on these experiments had multiple goals in mind. For starters, they simply wanted to see what was possible. How far could they push these genetic exchanges? What could they *do* with these bits and pieces of DNA?

There was also immense potential for basic research; taking a gene from one animal and putting it into another could help researchers learn more about how it worked and the role it played in development or disease. Finally, there were promising commercial applications, an opportunity to engineer animals whose bodies produced highly desired proteins or creatures with economically

valuable traits. (In one early project, for instance, researchers set out to make a leaner, faster-growing pig.)

Along the way, geneticists developed some neat tricks, including figuring out how to engineer animals that glowed. They knew that some species, such as the crystal jellyfish, had evolved this talent on their own. One moment, the jellyfish is an unremarkable transparent blob; the next it's a neon-green orb floating in a dark sea. The secret to this light show is a compound called green fluorescent protein (GFP), naturally produced by the jellyfish, which takes in blue light and reemits it in a kiwi-colored hue. Hit the jelly with a beam of blue light, and a ring of green dots will suddenly appear around its bell-shaped body, not unlike a string of Christmas lights wrapped around a tree.

When scientists discovered GFP, they began to wonder what would happen if they took this jellyfish gene and popped it into another animal. Researchers isolated and copied the jellyfish's GFP gene in the lab in the 1990s, and then the real fun began. When they transferred the gene into roundworms, rats, and rabbits, these animals also started producing the protein, and if you blasted them with blue light, they also gave off a green glow. For that reason alone, GFP became a valuable tool for geneticists. Researchers testing a new method of genetic modification can practice with GFP, splicing the gene into an organism's genome. If the animal lights up, it's obvious that the procedure worked. GFP can also be coupled with another gene, allowing scientists to determine whether the gene in question is active. (A green glow means the paired gene is on.)

Scientists discovered other potential uses, too. Zhiyuan Gong, a biologist at the National University of Singapore, wanted to use GFP to turn fish into living pollution detectors, swimming canaries in underwater coal mines. He hoped to create transgenic fish that would blink on and off in the presence of toxins, turning bright green when they were swimming in contaminated water. The first

step was simply to make fish that glowed. His team accomplished that feat in 1999 with the help of a common genetic procedure called microinjection. Using a tiny needle, he squirted the GFP gene directly into some zebrafish embryos. In some of the embryos, this foreign bit of biological code managed to sneak into the genome, and the fish gave off that telltale green light. In subsequent research, the biologists also made strains in red—thanks to a fluorescent protein from a relative of the sea anemone—and yellow, and experimented with adding these proteins in combination. One of their published papers showcases a neon rainbow of fish that would do Crayola proud.\*

To Richard Crockett, the co-founder of the company that sells GloFish, such creatures have more than mere scientific value—they have an obvious aesthetic beauty. Crockett vividly remembers learning about GFP in a biology class. He was captivated by an image of brain cells glowing green and red, thanks to the addition of the genes for GFP and a red fluorescent protein. Crockett was a premed student, but he was also an entrepreneur. In 1998, at the age of twenty-one, he and a childhood friend, Alan Blake, launched an online education company. By 2000, the company had become a casualty of the dot-com crash. As the two young men cast about for new business ideas, Crockett thought back to the luminescent brain cells and put a proposal to Blake: What if they brought the beauty of fluorescence genes to the public by selling glowing, genetically modified fish?

\* In 2005, Gong's team announced that they had successfully used GFP to create medaka—another species of small fish native to Asia—that did indeed turn green when they were exposed to environmental estrogens, synthetic chemicals that can disrupt the hormones of humans and other animals. In 2010, scientists at China's Fudan University achieved a similar breakthrough with zebrafish. Despite these advances, South Korea, host of the 2010 G20 Summit, took a far cruder approach when it employed a school of security fish to protect the world's leaders from contaminated water: If the goldfish swimming around in tanks of the water died, well, that might indicate a problem.

At first, Blake, who had no background in science, thought his friend was joking. But when he discovered that Gong and other scientists were already fiddling with fish, he realized that the idea wasn't far-fetched at all. Blake and Crockett wouldn't even need to invent a new organism—they'd just need to take the shimmering schools of transgenic fish out of the lab and into our home tanks.

The pair founded Yorktown Technologies to do just that, and Blake took the lead during the firm's early years, setting up shop in Austin, Texas. He licensed the rights to produce the fish from Gong's lab and hired two commercial fish farms to breed the pets. (Since the animals pass their fluorescence genes on to their offspring, all Blake needed to create an entire line of neon pets was a few starter adults.) He and his partner dubbed them GloFish, though the animals aren't technically glow-in-the-dark—at least, not the same way that a set of solar system stickers in a child's bedroom might be. Those stickers, and most other glow-in-the-dark toys, work through a scientific property known as phosphorescence. They absorb and store light, reemitting it gradually over time, as a soft glow that's visible when you turn out all the lights. GloFish, on the other hand, are fluorescent, which means that they absorb light from the environment and beam it back out into the world immediately. The fish appear to glow in a dark room if they're under a blue or black light, but they can't store light for later—turn the artificial light off, and the fish stop shining.

Blake was optimistic about their prospects. As he explains, "The ornamental fish industry is about new and different and exciting varieties of fish." And if new, different, and exciting is what you're after, what more could you ask for than an animal engineered to glow electric red, orange, green, blue, or purple thanks to a dab of foreign DNA? Pets are products, after all, subject to the same marketplace forces as toys or clothes. Whether it's a puppy or a pair of heels, we're constantly searching for the next big thing. Consider

the recent enthusiasm for "teacup pigs"—tiny swine cute enough to make you swear off pork chops forever.

Harold Herzog, a psychologist at Western Carolina University who specializes in human-animal interactions, has studied the way our taste in animals changes over time. When Herzog consulted the registry of the American Kennel Club, he found that dog breed choices faded in and out of fashion the same way that baby names do. One minute, everyone is buying Irish setters, naming their daughters Heather, and listening to "Bennie and the Jets"—welcome to 1974!—and then it's on to the next great trend. Herzog discovered that between 1946 and 2003, eight breeds—Afghan hounds, chow chows, Dalmatians, Dobermans, Great Danes, Old English sheepdogs, rottweilers, and Irish setters—went through particularly pronounced boom and bust cycles. Registrations for these canines would skyrocket, and then, as soon as they reached a certain threshold of popularity, people would begin searching for the next fur-covered fad.

Herzog identified a modern manifestation of our long-standing interest in new and unusual animals. In antiquity, explorers hunted for far-flung exotic species, which royal households often imported and displayed. Even the humble goldfish began as a luxury for the privileged classes. Native to Central and East Asia, the wild fish are usually covered in silvery gray scales. But ancient Chinese mariners had noticed the occasional yellow or orange variant wriggling in the water. Rich and powerful Chinese families collected these mutants in private ponds, and by the thirteenth century, fish keepers were breeding these dazzlers together. Goldfish domestication was born, and the once-peculiar golden fish gradually spread to the homes of less-fortunate Chinese families—and households elsewhere in Asia, Europe, and beyond.

As goldfish grew in popularity, breeders stepped up their game, creating ever more unusual varieties. Using artificial selection, they

created goldfish with freakish and fantastical features, and the world's aquariums now contain the fantail, the veiltail, the butterfly tail, the lionhead, the gooshead, the golden helmet, the golden saddle, the bubble eye, the telescope eye, the seven stars, the stork's pearl, the pearlscale, the black moor, the panda moor, the celestial, and the comet goldfish, among others. This explosion of types was driven by the desire for the exotic and exquisite—urges that we can now satisfy with genetically modified pets.

We can also use genetic engineering to create animals that appeal to our aesthetic sensibilities, such as our preference for brightly colored creatures. For instance, a 2007 study revealed that we prefer penguin species that have a splash of yellow or red on their bodies to those that are simply black and white. We've bred canaries, which are naturally a dull yellow, to exhibit fifty different color patterns. And before GloFish were even a neon glint in Blake's eye, pet stores were selling "painted" fish that had been injected with simple fluorescent dyes. With fluorescence genes, we can make a true rainbow of bright and beautiful pets.\*

Engineered pets also fit right into our era of personalization. We can have perfume, granola, and Nikes customized to our individual specifications—why not design our own pets? Consider the recent rise of designer dogs, which began with the Labradoodle, a cross between a Labrador retriever and a standard poodle. Though there's no telling when the first Lab found himself fancying the well-groomed poodle down the street, most accounts trace the

\* Not all aesthetic alterations are created equal. Scientists have created beagles that turn ruby under ultraviolet light—by transferring a sea anemone gene into the dogs—but these GloDogs, as it were, are disturbing to gaze upon. They would surely be a harder sell than GloFish, perhaps because cough-syrup red is a color that never naturally occurs in the canine kingdom. Since nature itself has created some fish that are red and orange, however, artificially adding one of these hues to an aquarium resident doesn't seem so jarring.

origin of the modern Labradoodle to Wally Conron, the breeding director of the Royal Guide Dog Association of Australia. In the 1980s, Conron heard from a blind woman in Hawaii, who wanted a guide dog that wouldn't aggravate her husband's allergies. Conron's solution was to breed a Lab, a traditional seeing-eye dog, with a poodle, which has hypoallergenic hair. Other breeders followed Conron's lead, arranging their own mixed-breed marriages. The dogs were advertised as providing families with the best of both worlds—the playful eagerness of a Lab with the smarts and hypoallergenic coat of the poodle. The rest, as they say, is history. The streets are now chock-full of newfangled canine concoctions: puggles (a pug-beagle cross), dorgis (dachshund plus corgi), and cockapoos (a cocker spaniel—miniature poodle mix). There's even a mini Labradoodle for doodle lovers without lots of space.

Tweaking the genomes of our companions allows us to create a pet that fulfills virtually any desire—some practical, some decidedly not. When I set out to get a dog, I thought I had settled on the Cavalier King Charles spaniel: small, soft, and bred for companionship. Then I discovered a breeder who was crossing Cavaliers with miniature poodles, yielding the so-called Cavapoo. I was sold. I loved the scruffier, shaggier hair of the Cavapoo, and given what I knew about biology, I figured that a hybrid was less likely to inherit one of the diseases that plague perilously inbred canines. A dog that didn't shed would be an added bonus. Plus, poodles have a reputation for being brainy, and I'm an overachiever; if I was going to get a dog, I wanted to be damn sure he'd be the valedictorian of his puppy kindergarten class.

The hitch: Even the most careful selective breeding is a rough science. Sure, Labs are friendly and poodles are intelligent, but just letting them go at it doesn't guarantee that their puppies will exhibit the best of both breeds. Milo, the Cavapoo I eventually brought home, looks almost entirely like a spaniel, and as for a nonshedding

coat, his health, and those famous poodle smarts? Well, my couch is covered with dog hair, Milo has a knee problem common in purebred Cavaliers, and I'm pretty sure he got the spaniel brain. So much for my plan to outsmart nature.

When I'm ready for my next pet, the landscape could be radically different. Social Technologies, a trend forecasting firm in Washington, D.C., issued a report on the commercial prospects for genetically modified pets. "Through advances in genetic modification," the report said, "biotechnology labs could join kennels and animal shelters as a source for the perfect pet... Initially a luxury, pet personalization would become available to the general public as the technologies involved become more mature."

Indeed, why bother creating clumsy crosses when we can edit genes directly? A company called Felix Pets, for example, is attempting to engineer cats that are missing a gene called *Fel d 1*, which codes for a protein that triggers human allergies.\* And that's just the beginning. What if you could order up a fish created in your alma mater's trademark palette or dogs and cats with custom patterns on their coats? Or there's the ultimate designer pet, proposed by Alan Beck, director of Purdue's Center for the Human-Animal Bond: "If we're going to come up with genetically engineered animals, we might be able to come up with an animal that loves only you."

Transgenic pets will have to clear some hurdles before they make it to market. The Food and Drug Administration considers a new gene that is added to an organism to be a "drug," and regulates

\* Another company, Lifestyle Pets, already sells what it claims are hypoallergenic cats. The cats, which go for nearly \$7,000 a pop, are not products of direct genetic manipulation. Instead, the company says it has merely identified and bred cats with a natural mutation in *Fel d 1*. However, it remains unclear whether Lifestyle Pets has truly cracked the hypoallergenic code; controversy has long swirled around the company and its scientific claims.

altered animals under the Federal Food, Drug, and Cosmetic Act. Companies seeking approval to sell an engineered animal must demonstrate that the transgene has no ill effects on the animal itself. If the animal will be a source of food, companies must also demonstrate that it is safe for human consumption.

Regulators also evaluate how a genetically modified organism might affect the environment if it happened to make its way into the wild. Escape has been a concern since the first genetically engineered bacteria were created in the early 1970s. The scientists of that era worried about what might happen if they inadvertently created a dangerous superbug and it slipped out under the laboratory door. Biologists convened twice—at the Asilomar conferences of 1973 and 1975—to discuss these risks. In 1975, they drew up a document that encouraged their colleagues to exercise caution and use "biological and physical barriers" to ensure that novel organisms didn't break free from the lab. The National Institutes of Health issued guidelines stipulating such safeguards in 1976 and has periodically updated its recommendations over the years.

Though these containment strategies are now routine, they aren't foolproof, and ecologists continue to worry about engineered organisms ending up in the wild. Altered animals could "pollute" the gene pool by breeding with their free-range cousins, or snatch food and resources away from native organisms. In theory, laboratory manipulation could make a fish more likely to thrive in the big, wide world, and such Frankenfish could take over natural waterways, to the detriment of other species.

This very possibility has been part of the high-profile debate over the most famous (or infamous) transgenic fish: a fast-growing Atlantic salmon that AquaBounty, a Massachusetts firm, is trying to bring to market in the United States. Atlantic salmon normally produce growth hormone only in the summer, but the AquaAdvantage fish have been engineered to crank out the hormone no matter what

the season. The secret is a bit of biological code borrowed from the ocean pout, an eel-like fish that lives in frigid water. To keep its cellular machinery from icing over, the slithery fish produces its own antifreeze. The pout's antifreeze gene is normally attached to a sequence of regulatory DNA called a "promoter." Icy temperatures activate the promoter, which turns the gene on, triggering the ocean pout to start cranking out the antifreeze. The cold-sensitive promoter, however, can be attached to all sorts of different genes, and to create the AquaBounty fish, scientists linked the promoter to a growth-hormone gene taken from the Chinook salmon. Then they slipped the entire construct into Atlantic salmon. As a result, in these salmon, cold temperatures prompt the production of growth hormone, and the fish reach their adult sizes faster than their unaltered counterparts. The genetic modification shaves a year and a half off the time between when a salmon hatches and when it's ready to garnish your bagel.

It's a clever bit of biological reprogramming, but AquaBounty has attracted vocal critics, many of whom fear that if the big bruisers from the lab escape, they could wreak havoc on wild salmon populations. To address these concerns—and reassure nervous regulators—AquaBounty is building several security measures into its production plans. It will breed fish in a secure facility in Canada and then raise the young in confined tanks situated in the highlands of Panama, far from their natural marine environment. The company also plans to produce only sterile female fish—incapable of passing their genes on even if they did somehow end up on the lam.

Though many scientists have concluded that there is little risk of the supersalmon escaping and staging some sort of wild coup, AquaBounty is still trying to win over regulators. The company first approached the FDA about its fish in 1993, and applied for formal approval in 1995. Despite deciding that the fish are low risk, the FDA has not yet ruled on whether they will be allowed on the mar-

ket. (If the salmon are approved, they would become the first GM animal to officially enter the world's food supply.)

As Alan Blake prepared to bring GloFish to market, he studied the regulatory challenges that have hobbled AquaBounty. Blake wasn't sure what federal agencies would do about genetically modified *pets*, but he didn't want to take any chances, so he began calling government officials and asking whether they'd have concerns about GloFish. He told regulators that the fish were designed to be companions, not food, and reassured them that scientists believed the animals posed a negligible risk to the environment. Wild zebrafish, he told them, spend their time in the tropics, not the chilly waters of North America. Conventional zebrafish have been sold as pets in the United States for decades, and they have never been able to survive an aquarium jailbreak long enough to establish a wild population. The water is simply too cold, and the fluorescent varieties are even less likely to make a go of it—the data suggest that GloFish are more sensitive to cold temperatures, less successful at reproducing, and, one suspects, more visible to predators, with their big, neon EAT ME signs.

Of course, there is no such thing as zero risk, but Perry Hackett, a geneticist who studies zebrafish at the University of Minnesota, puts the danger posed by GloFish this way: "What are the odds that all the air molecules will rush up into a corner of the room you're sitting in and you'll suffocate? That for whatever reason, just at random, they all happen to collect just in one corner?" Such a scenario is theoretically possible, but it's so unlikely that we don't worry about it. As Hackett says, "We don't sit around with oxygen tanks by our desks."

Federal officials didn't register any serious objections in their conversations with Blake, and by the summer of 2003, he thought he had his bases covered. He had consulted with scientific and legal experts. The licenses to produce the neon Nemos were in hand. And



the fish farmers were ready to start churning them out. Blake set a launch date of January 2004, but then California caught him by surprise. The state's Fish and Game Commission instituted a regulation prohibiting the production and sale of all genetically modified fish. Anyone who wanted to breed, buy, sell, or own these organisms needed to appear before the commission and request a formal exemption.

That fall, Blake was busy preparing for his hearing before the commission when a technical glitch suddenly made the company's password-protected website available to all eyes. The press got wind of Blake's Seussian fish, and within a week, the animals were discussed everywhere from National Public Radio to Al-Jazeera. Many publications ran anxiety-provoking stories, but the fearmongering award winner had to be a *New York Times* headline: WHEN FISH FLUORESCES, CAN TEENAGERS BE FAR BEHIND? As the story put it, "This is the tipping point, when the world irrevocably turns toward the science-fiction fantasies of writers . . . No doubt humans could be made to glow if parents with foresight knew that one day they would be desperately trying to find their middle school child at a dark and crowded school dance."

The stories made GloFish seem like monsters, harbingers of some sort of ethical or scientific apocalypse. Indeed, the genome can seem like a set of commandments—handed down and carved into stone—and fiddling with it makes us nervous. Selective breeding has become an accepted practice, but our ability to root around in the genome directly and move pieces of DNA between different species is still unsettling. "These are techniques that are advancing the threshold of human power over other species," says Richard Twine, a sociologist and bioethicist at Lancaster University. "It's a way of increasing the continuum of control over the animal and genotype and phenotype. There's an intensification, a new power that we didn't have before." What's more, once GloFish officially went on

sale, they'd be available to anyone with five dollars, meaning that organisms once confined to pulpy science fiction novels could be living in your neighbor's den. With the launch of GloFish, biotechnology would come to our houses and knock on our front doors.

The California Fish and Game Commission seemed acutely aware of these concerns when it convened to discuss GloFish in December 2003. Unless you are an expert on the cold calculus of culling wild turkeys or an aficionado of the tender lovemaking habits of the New Zealand mud snail, Fish and Game meetings can be brain-deadening experiences. But on this particular afternoon, there would be a captivating showdown over our biotechnological future.

When Blake came to the podium for his opening remarks, he had a slightly bewildered air about him, like a straight-A student who suddenly finds himself called to the principal's office. He was well-mannered and deferential, peppering his comments with "sir"s and "gentlemen"s. As he spoke, it was obvious that he had done his homework. All the scientists that he had consulted—as well as the experts that the Department of Fish and Game had conferred with before the hearing—had concluded that GloFish were safe. But Blake had made a critical miscalculation: that the data would be enough.

GloFish may have been a laboratory triumph, but debates over biotechnology rarely come down to the science. According to public opinion polls, only 27 percent of Americans believe that the government should base its decisions about genetic engineering purely on science. Compare that with the 63 percent who think such decisions should take "moral and ethical factors" into account. That's just what the California commission did. Commissioner Sam Schuchat told Blake that he had already done a lot of thinking about whether GloFish should be sold in California. He'd even called his rabbi to discuss his concerns. "The question for me became an ethical question," Schuchat said at the hearing. "Here we are, playing around with the genetic basis of life, creating new organisms that



don't exist. Now it is true that we human beings have been doing that for tens of thousands of years. But I guess at the end of the day, I don't think it's right to produce a new organism just to be a pet. I look at this issue in front of us and I think to myself, 'So, what's next? Pigs with wings? Pink horses?'

"Let me be clear," he continued. "I'm not opposed to genetically modified organisms. But I don't think it is a good idea to employ this technology for what I would characterize as frivolous purposes . . . To me, this seems like an abuse of the power that we have over life, and I'm not prepared to go there today."

Blake had heard this objection before from some of the scientists he first consulted about his business plan. When Eric Hallerman, a fish geneticist at Virginia Tech, heard about GloFish, he worried that they were "a fairly trivial use of technology." But Hallerman, who has advised the federal government about risks that accompany genetically modified animals, overcame his initial skepticism, even joining the Yorktown Technologies Scientific Advisory Board. As Hallerman explains, when it comes to GloFish, "there's no harm being done, and there's fairly few enterprises that humans engage in, including agriculture, in which no harm is being done."

Let's not forget that even selective breeding can do harm. Those ornamental goldfish varieties that we've created to have eerie, unearthly eyes—enlarged and bulging, or covered by enormous growths, or positioned to look up toward the sky—can be nearly blind. From an ethical standpoint, isn't a fully functional transgenic fish preferable to an artificially selected but severely handicapped one?\*

\* We've also saddled dog breeds with all sorts of inherited diseases, and the English bulldog has been pushed so far by human selection that it is literally handicapped. The breed's massive head doesn't fit through the birth canal, and pups are usually born via cesarean section. Their snouts are so short that the dogs can barely breathe—they suffer from sleep apnea and a lifetime of oxygen deprivation. These breathing

Not, apparently, to the California commissioners. After they finished querying Blake, they voted, three to one, to deny his request. Commissioner Michael Flores was the lone dissenter. "We have a gentleman out here who's gone to the scientific community, those that are very precautionary, and they say that there's no risk," he said at the meeting. "So we're going to ignore that science, and that has me a little bit concerned." But Flores's single vote wasn't enough, and the objections of his colleagues meant that there would be no GloFish in the Golden State.

California could have been a huge market for Blake, who was disappointed with the ruling, but there were still forty-nine other states to sell in, and just days after the California commission rejected GloFish, the FDA released an official statement on the pets. It read, in full: "Because tropical aquarium fish are not used for food purposes, they pose no threat to the food supply. There is no evidence that these genetically engineered zebra danio fish pose any more threat to the environment than their unmodified counterparts which have long been widely sold in the United States. In the absence of a clear risk to the public health, the FDA finds no reason to regulate these particular fish."

A few opponents refused to accept the FDA's ruling as the final word. Just after GloFish hit pet stores in January 2004, the International Center for Technology Assessment and the Center for Food Safety—two affiliated nonprofits that have raised concerns about a variety of biotechnologies—filed a lawsuit. They alleged that the

difficulties also mean that the animals have trouble regulating their own body temperature, and many suffer early deaths from respiratory or heart failure. "If bulldogs were the products of genetic engineering, there would be protest demonstrations throughout the Western world, and rightly so," James Serpell, the director of the Center for the Interaction of Animals and Society at the University of Pennsylvania, once wrote. "But because they have been generated by anthropomorphic selection, their handicaps not only are overlooked but even, in some quarters, applauded."

FDA and the U.S. Department of Health and Human Services had shirked their legal duty to subject GloFish to a thorough review. In an attempt to convince the court that they had the right to sue, the plaintiffs constructed an unconventional argument. How had GloFish harmed them? Well, among other things, they said, the sale of the freaks of nature could lead to "aesthetic injury from viewing genetically engineered GloFish and other animals in aquaria..." The suit was eventually dismissed, but the "aesthetic injury" argument was a testament to just how desperate some opponents were to keep the animals out of pet shops. (Aesthetic injury? If that's a valid legal argument, I've got a couple of lawsuits I'd like to file. Mexican hairless dog. I'm looking at you.)

The aesthetic-injury argument apparently didn't find much traction with the public either, because GloFish, and their Kodak-worthy colors, are a hit, available in all of America's major pet store chains. (Yorktown Technologies sells its fish only in the United States, although the Taiwanese company Taikong sells its own version of the paint-box pets in Asia. Though he'd love to sell to customers in Canada and Europe, Blake doesn't want to tangle with these jurisdictions' ultratight restrictions on genetically modified organisms.) At first, Yorktown Technologies sold only red GloFish, but the company added green and orange varieties in 2006 and blue and purple in 2011. In 2012, the company introduced an entirely new fish: a white skirt tetra (*Gymnocorymbus ternetzi*) genetically modified to fluoresce bright green.\* Petco, PetSmart, and Walmart also sell GloFish "kits," special tanks that come equipped with blue lights designed to bring out the fish's brilliance.

\* Yorktown Technologies conducted "comprehensive" studies of the glowing tetra, Blake says, which revealed that the fluorescent tetra were less environmentally fit—and thus less likely to survive in the wild—than their unmodified counterparts. The company submitted this data to the FDA, which raised no objections to commercial sale of the fish, Blake says.

"We have e-mails from customers who love the fish," Blake tells me. "We've gotten thousands and thousands of e-mails and, on average, every year, we get—four? five?—e-mails from people that are expressing negativity. There are probably more people that claim to see Elvis flying a UFO in any major U.S. city every year."

Once GloFish hit the market, their fate was determined not by some abstract debate over biotechnology but rather by public demand. Customers simply like the fish. The success of GloFish is all the more remarkable in light of the public opinion surveys that show that most Americans aren't fans of lab-grown companions. (In one survey, 40 percent of respondents said that creating disease-resistant animals—such as chickens safe from the ravages of avian flu—was a "very good reason" to meddle with the genome. Compare that with the 4 percent who said that creating new pets was a "very good reason" to do so.) Is it possible that GloFish have changed our minds? Maybe there are some people out there who went into pet stores expecting something monstrous and came away thinking that GloFish were not only harmless but actually downright cool. It's what can happen when we get the opportunity to have close, personal encounters with biotechnology.

And it's one reason Blake takes his responsibilities seriously. Yes, he has a financial interest in GloFish's success, but he also knows that he has an opportunity to help shape public opinion. He hopes that GloFish will be a bright, shining example, proof that species engineering doesn't have to be so scary. "Biotechnology is often demonized," Blake says. "And then you see this tiny little fish, just swimming around, as happy as can be."

Are the fish happy? Are fish even capable of "happiness"? These are the questions I ponder as I stand, once again, at Petco, looking into a tank of glowing fish. It has occurred to me that just about the only

thing I haven't done in the GloFish research department is invite them into my home. So here I am, ready to take the plunge. I grab the special GloFish aquarium and am about to pick out some plain gray stones to put in the bottom of the tank, but my boyfriend spots a bag of mixed gravel in hues that look like they belong on a tie-dyed T-shirt. "You should get those," he says.

"Won't that be tacky?"

"You're getting genetically modified, fluorescent fish," he says. "Don't you think that ship has sailed?"

I might as well go all in. I grab the fluorescent gravel and some neon plastic plants.

Then it's over to the corner tank that GloFish call home. They're swimming around in a hallucinogenic jumble, and I ask a clerk to corral six of them for me: two Electric Greens, two Starfire Reds, and two Sunburst Oranges. (At \$5.99 each, I am stocking an aquarium with next-gen pets for less than \$40—far less than the cost of my Cavapoo.) An employee plops the fish into a plastic bag filled with water. I hold the bag up to my face and come eye-to-eye with the doctored fish. They continue their openmouthed stares, hovering silently in the water. I don't exactly fear for the fate of the Earth. ("You'd think they were six feet long with fangs and they'd bite your head off, the way they've been portrayed," Blake once told me.)

I tote them home and set up the tank up in my living room. Under the blue light coming from the bulb, the GloFish gleam like jewels. I don't know if they're happy, but they certainly don't appear to be suffering. Neither am I—it's entrancing to watch them swimming around, a kaleidoscope in constant motion. These fish may be frivolous, but they're just a teaser, a preview of the coming attractions. If we can get black-and-white fish to glow neon red, green, and orange, what else can we get animal bodies to do?

## 2. Got Milk?



When scientists first learned how to edit the genomes of animals, they began to imagine all the ways they could use this new power. Creating brightly colored novelty pets was not a high priority. Instead, most researchers envisioned far more consequential applications, hoping to create genetically engineered animals that saved human lives. One enterprise is now delirious on this dream. Welcome to the world of "pharming," in which simple genetic tweaks turn animals into living pharmaceutical factories.

Many of the proteins that our cells crank out naturally make for good medicine. Our bodies' own enzymes, hormones, clotting factors, and antibodies are commonly used to treat cancer, diabetes, autoimmune diseases, and more. The trouble is that it's difficult and expensive to make these compounds on an industrial scale, and as a result, patients can face shortages of the medicines they need. Dairy animals, on the other hand, are expert protein producers, their udders swollen with milk. So the creation of the first transgenic mammals—first mice, then other species—in the 1980s gave